

Remarks

The Office Action mailed October 1, 2004 has been received and reviewed. Claim 7 has been canceled, claims 1-6 and 54-61 having been amended, and claims 62-69 having been added, the pending claims are claims 1-6, 21-43, and 54-69. Claims 21-43 having been withdrawn from consideration by the Examiner as being drawn to a non-elected invention, the claims currently under consideration are claims 1-7 and 54-69.

The specification has been amended at page 32, line 20 to correct an inadvertent recitation of a hyperlink. No new matter has been added.

Claims 1-6 and 54-61 have been amended to recite a purified polypeptide, which is supported by the specification in general, and specifically, for example, at page 2, line 32; page 12, line 22; and the working examples (e.g., pages 45-49). Claims 54-61 have also been clarified by reciting "a contiguous stretch of amino acids," which is supported by the specification at, for example, page 32, lines 28-31.

New claims 62-69 are generally supported by the specification and originally filed claims. Specifically, the end points of the polypeptide recited in new claim 62 are supported by the specification at, for example, page 16, lines 23-24 ("Domains 1 and 2 are responsible for binding of the flavin adenine dinucleotide (FAD) cofactor "), line 29 ("Domain 1 (residues 14-98) of *S. aureus* MurB"), and line 31 ("The second domain of *S. aureus* MurB (residues 101-229)"). The end points of the polypeptide recited in new claim 66 are supported, for example, by the specification at, for example, page 16, line 24 ("domain 3 is responsible for substrate binding"); and page 16, line 33 to page 17, line 1 ("domain 3 of the *S. aureus* enzyme (residues 230-316)").

Reconsideration and withdrawal of the rejections are respectfully requested.

Objection to the Drawings

The Examiner objected to the drawings, and alleged that the first sheet of Figures 4 and 12 do not correspond to the descriptions of Figures 4 and 12 in the specification (e.g., pages 10 and 12, respectively). The alleged lack of correspondence is not clear to Applicant as discussed herein below.

The description of Figure 4 on page 10 recites that "Figure 4 lists the atomic structure coordinates for molecule *S. aureus* Mur B as derived by x-ray diffraction from a crystal of that complex" (lines 7-8). Figure 4 includes a single listing of atomic structure coordinates that is 46 pages in length (i.e., Fig. 4A-1 through Fig. 4A-46). The first sheet of Fig. 4 is a conventional method of clarifying that the listing is intended to be a continuous listing, with the pages read consecutively.

Similarly, the description of Figure 12 on page 12 recites that "Figure 12 lists the structure factors and multiple anomalous dispersion phases for the crystal structure of *S. aureus* Mur B" (lines 4-5). Figure 12 includes a single listing of structure factors and multiple anomalous dispersion phases that is 565 pages in length (i.e., Fig. 12A-1 through Fig. 12A-565). The first sheet of Fig. 12 is a conventional method of clarifying that the listing is intended to be a continuous listing, with the pages read consecutively. The first sheet of Fig. 12 has been amended to correct a typographical error, so as to correctly recite Fig. 12A-1 through Fig. 12A-565.

Reconsideration and withdrawal of the objection to the drawings are respectfully requested. In the event that the objection to the drawings is maintained, clarification of the specific nature of the objection is respectfully requested in the next Official Communication.

Objection to the Specification

The Examiner objected to the specification for having a hyperlink embedded in the specification. The specification having been amended at page 32, line 20, Applicant respectfully submits that the objection has been rendered moot.

Applicant respectfully requests reconsideration and withdrawal of the objection to the specification.

Rejection under 35 U.S.C. §101

The Examiner rejected claims 1-7 and 54-61 under 35 U.S.C. 101 for being directed to non-statutory subject matter. Claim 7 has been canceled. Claims 1-6 and 54-61 have been amended to recite "purified," as kindly suggested by the Examiner. Applicant respectfully submits that the rejection has been obviated.

Reconsideration and withdrawal of the rejection under 35 U.S.C. §101 are respectfully requested.

Rejection under 35 U.S.C. §112, Second Paragraph

In paragraph 14 of the Office Action mailed October 1, 2004, the Examiner listed claims 1-6 and 51-55 as being rejected under 35 U.S.C. §112, second paragraph. However, claims 51-53 have been canceled. For the purposes of this response, Applicant is assuming that the Examiner intended to list claims 1-7 and 54-61, which are all listed in the body of the rejection, as being rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. If this assumption is not correct and the rejection is maintained, the Examiner is invited to clarify the rejection in the next Official Communication. Applicant respectfully traverses the rejection.

First, the Examiner asserted that claims 1-6, 55-57, and 59-61 are indefinite for reciting amino acids listed in a table without a reference to an amino acid sequence. Applicant respectfully disagrees.

Applicant respectfully submits that claims 1-6, 55-57, and 59-61 (as amended) recite amino acids listed in the indicated table, wherein the three-dimensional configuration of the amino acids is defined relative to the structure coordinates listed in Figure 4. Thus, Applicant

respectfully submits that claims 1-6, 55-57, and 59-61 (as amended) are definite without reciting an amino acid sequence.

Second, the Examiner rejected claim 7 as indefinite. Claim 7 having been canceled, the rejection has been rendered moot.

Finally, the Examiner asserted that "[c]laims 55-57 and 59-61 are confusing in that the protein of claim 54 or 58 is not limited to having the amino acids listed in Tables 1-6" and that "claims 54 and 58 can be interpreted as a peptide with as few as two amino acids" (paragraph 14d of the Office Action mailed October 1, 2004). Applicant respectfully traverses the rejection.

Applicant respectfully submits that it is clear to one of skill in the art that claim 54 relates to a polypeptide consisting of a portion of *S. aureus* MurB (SEQ ID NO:1), wherein the portion consists of a contiguous stretch of amino acids starting at one of amino acids 37 to 42 and ending at one of amino acids 310 to 312 of SEQ ID NO:1; and that claim 58 relates to a polypeptide consisting of a portion of *S. aureus* MurB (SEQ ID NO:1), wherein the portion consists of a contiguous stretch of amino acids starting at one of amino acids 42 to 155 and ending at one of amino acids 274 to 309 of SEQ ID NO:1. Thus, Applicant respectfully submits that one of skill in the art would not interpret claims 54 and 58 as relating to a peptide with as few as two amino acids, as suggested by the Examiner. However, in the interest of expediting the prosecution of the present application, claims 54 and 58 have been amended, and the rejection is obviated.

Reconsideration and withdrawal of the rejections under 35 U.S.C. §112, second paragraph, are respectfully requested.

Rejections under 35 U.S.C. §112, First Paragraph

NEW MATTER REJECTION

The Examiner rejected claims 54-61 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and alleged that claims 54-61 include new matter. Specifically, the Examiner alleged that the starting and ending points of the polypeptides recited in claims 54 and 58 are not supported by the originally filed specification. Applicants respectfully traverse the rejection.

Independent claims 54 and 58 are each directed to a polypeptide consisting of a portion of *S. aureus* MurB (SEQ ID NO:1) that includes a binding pocket. *See, for example*, Trilateral Project WM4 on *Comparative study on "protein 3-dimensional (3-D) structure related claims,"* Annex 3, Case 5, [Claim 2] (http://www.uspto.gov/web/tws/wm4/pdf/wm4_3d_annex_3.pdf).

Independent claim 54 (as amended) recites a polypeptide consisting of a portion of *S. aureus* MurB (SEQ ID NO:1), wherein the portion consists of a contiguous stretch of amino acids starting at one of amino acids 37 to 42 and ending at one of amino acids 310 to 312 of SEQ ID NO:1; and that claim 58 (as amended) recites a polypeptide consisting of a portion of *S. aureus* MurB (SEQ ID NO:1), wherein the portion consists of a contiguous stretch of amino acids starting at one of amino acids 42 to 155 and ending at one of amino acids 274 to 309 of SEQ ID NO:1. Applicants respectfully submit that the claimed polypeptides are adequately supported by the originally filed specification.

Specifically, claim 54 is directed to fragments of *S. aureus* MurB (SEQ ID NO:1) that include amino acid residues in the FAD binding pocket as listed, for example, in Tables 1-3. As such, the smallest fragment possible that includes all the polypeptide amino acids listed in Tables 1, 2, or 3 must necessarily start at the smallest numbered residues in Tables 1-3 (i.e., amino acids 37, 41, or 42 in Tables 3, 2, or 1, respectively) and end at the largest numbered residues (i.e., amino acids 310, 312, or 312 in Tables 1, 2, or 3, respectively). Thus, Applicant respectfully submits that claim 54, which recites a contiguous stretch of amino acids starting at one of amino acids 37 to 42 and ending at one of amino acids 310 to 312 of SEQ ID NO:1, is adequately supported by the specification.

Similarly, claim 58 is directed to fragments of *S. aureus* MurB (SEQ ID NO:1) that include amino acid residues in the substrate binding pocket as listed, for example, in Tables 4-6. As such, the smallest fragment possible that includes all the polypeptide amino acids listed in Tables 4, 5, or 6 must necessarily start at the smallest numbered residues in Tables 4-6 (i.e., amino acids 42, 82, or 155 in Tables 6, 5, or 4, respectively) and end at the largest numbered residues (i.e., amino acids 274, 308, or 309 in Tables 4, 5, or 6, respectively). Thus, Applicant respectfully submits that claim 58, which recites a contiguous stretch of amino acids starting at one of amino acids 42 to 155 and ending at one of amino acids 274 to 309 of SEQ ID NO:1, is adequately supported by the specification.

WRITTEN DESCRIPTION

The Examiner rejected claims 1-7 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner alleged that a representative species (e.g., *S. aureus* MurB of SEQ ID NO:1) is inadequate to support the claimed genus of molecules or molecular complexes. Claim 7 having been canceled, and claims 1-6 having been amended, Applicant respectfully traverses the rejection as applied to claims 1-6 (as amended).

"The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice . . . , reduction to drawings . . . , or by disclosure of relevant identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. . . .

[T]here may be situations where one species adequately supports a genus." M.P.E.P.

§2163(II)(A)(3)(a)(ii).

Without more, the disclosure of one species (e.g., *S. aureus* MurB of SEQ ID NO:1), arguably may not support a genus of purified polypeptides as recited in claims 1-6 (as amended). However, the present claims provide more than the bare sequence of one protein. Applicants respectfully submit that the present claims satisfy the written description requirement of 35 U.S.C. §112, first paragraph, for at least the reasons discussed herein below.

Claims 1-3 (as amended) each recite that the claimed purified polypeptide includes at least a portion of an *S. aureus* MurB or MurB-like FAD binding pocket. Such FAD binding pockets are described in the specification by identifying characteristics including, for example, structure (e.g., Figures 6-8; Tables 1-3 and Figure 4; and page 16, line 21 to page 24, line 10). Further, the specification provides guidance for one of skill in the art to determine, for candidate polypeptides, suitable homology to SEQ ID NO:1 (e.g., page 32, line 1 to page 37, line 10).

Similarly, Claims 4-6 (as amended) each recite that the claimed purified polypeptide includes at least a portion of an *S. aureus* MurB or MurB-like substrate binding pocket. Such substrate binding pockets are described in the specification by identifying characteristics including, for example, structure (e.g., Figures 6-7 and 9; Tables 4-6 and Figure 4; and page 16, line 21 to page 24, line 10). Further, the specification provides guidance for one of skill in the art to determine, for candidate polypeptides, suitable homology to SEQ ID NO:1 (e.g., page 32, line 1 to page 37, line 10).

Thus, Applicant respectfully submits that claims 1-6 are adequately supported by the specification to meet the written description requirement of 35 U.S.C. §112, first paragraph.

ENABLEMENT

The Examiner rejected claims 1-7 and 54-61 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, while acknowledging that the specification enables the *S. aureus* MurB polypeptide of SEQ ID NO:1, the Examiner alleged that the specification

does not reasonably provide enablement for all molecules or molecular complexes as encompassed by claims 1-7 and 54-61. Claim 7 having been canceled, and claims 1-6 and 54-61 having been amended, Applicant respectfully traverses the rejection as applied to claims 1-6 and 54-61 (as amended).

"A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." M.P.E.P. §2164.04. "As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied."

M.P.E.P. §2164.01(b). "For a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art (in view of level of skill, state of the art and the information in the specification) would expect the claimed genus could be *used* in that manner without undue experimentation. Proof of enablement will be required for other members of the claimed genus only where adequate reasons are advanced by the examiner to establish that a person skilled in the art could not *use* the genus as a whole without undue experimentation." M.P.E.P. §2164.02, paragraph entitled "WORKING EXAMPLES AND A CLAIMED GENUS" (emphasis added). "[E]ven in unpredictable arts, a disclosure of every operable species is not required." M.P.E.P. §2164.03.

First, Applicant respectfully submits that claims 54-61 (as amended) are fully enabled by the specification. Claims 54-61 (as amended) recite polypeptides ***consisting of*** a portion of *S. aureus* MurB (SEQ ID NO:1), wherein the portion consists of a contiguous stretch of amino acids with the recited starting and ending points. Thus, Applicant respectfully submits that the Examiner's assertion that claims 54-61 encompass fragments of as few as two amino

acids (i.e., fragments that are too small to generate antibodies to SEQ ID NO:1) has been rendered moot in view of the clarified meaning of claims 54-61 (as amended).

Further, Applicant respectfully submits that claims 1-6 (as amended) are fully enabled by the specification. Applicant thanks the Examiner for acknowledging that the specification enables the *S. aureus* MurB polypeptide of SEQ ID NO:1. Applicant further submits that the specification also enables SEQ ID NO:1, wherein at least one methionine is replaced with selenomethionine (e.g., page 13, lines 13-29; page 36, lines 3-12; and page 45, line 13 to page 47, line 27). Moreover, claims 1-6 have been amended to recite purified polypeptides, and Applicant respectfully submits that the specification provides guidance for one of skill in the art to make and use the genus of polypeptides recited in claims 1-6. The specification describes methods of making and purifying polypeptides (e.g., page 45, line 13 to page 47, line 27), methods of crystallizing such polypeptides (e.g., page 12, lines 22-32; and page 47, line 29 to page 48, line 6), and methods of determining the crystal structure of such polypeptides (e.g., page 13, lines 8-29; and page 48, line 9 to page 49, line 27). Moreover, although not required, the specification includes working examples of methods for making, purifying, crystallizing, and determining the crystal structure of *S. aureus* MurB (e.g., pages 45-49). The specification also provides methods of using crystals of the claimed polypeptides (e.g., homology modeling and rational drug design, page 37, line 12 to page 44, line 5). Finally, the Examiner has not provided any reason to doubt the objective truth of the disclosure provided in the specification.

Moreover, Applicant respectfully submits that one of skill in the art, using the disclosure provided in the specification (including the working examples), would be able to make and use the entire scope of the invention as recited in claims 1-6 (as amended). For example, Applicants' Representatives respectfully submit that the present disclosure of structure coordinates (e.g., Table 4) and structure factors and multiple anomalous dispersion phases (e.g., Table 12) for the crystal structure of *S. aureus* MurB would allow one of skill in the art to make

and use purified polypeptides as recited in claims 1-6. Thus, Applicants respectfully submit that claims 1-6 (as amended) are fully enabled by the specification.

Reconsideration and withdrawal of the rejections under 35 U.S.C. §112, first paragraph, are respectfully requested.

Rejections under 35 U.S.C. §102

The Examiner rejected claims 1-7 under 35 U.S.C. §102(e) as being anticipated by Wallis et al. (U.S. Patent No. 6,225,098 B1) or Database GenBank Accession Number P08373. Claim 7 having been canceled, and claims 1-6 having been amended, Applicant respectfully traverses the rejections as applied to claims 1-6 (as amended).

For anticipation to occur, a prior art disclosure must put the public in possession of the invention:

"In determining that quantum of prior art disclosure which is necessary to declare an applicant's invention 'not novel' or 'anticipated' within section 102, the stated test is whether a reference contains an 'enabling disclosure'. . . ." *In re Hoeksema*, 399 F.2d 269, 158 USPQ 596 (CCPA 1968). A reference contains an "enabling disclosure" if the public was in possession of the claimed invention before the date of invention. "Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention." *In re Donohue*, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985).

M.P.E.P. §2121.01. Applicant respectfully submits that each cited document fails to put the public in possession of the claimed invention.

Claims 1-6 (as amended) each recite a binding pocket being defined by a set of points relative to the structure coordinates listed in Figure 4 (i.e., three-dimensional structural information). Notably, neither of the cited documents discloses such three-dimensional structural information as recited in claims 1-6 (as amended). Moreover, neither of the underlying documents for Database GenBank Accession Number P08373 (i.e., Howard et al.,

Gene, 35:321-331 (1985); and Pucci et al., *J. Bacteriology*, 174:1690-1693 (1992)) discloses such three-dimensional structural information as recited in claims 1-6 (as amended).

Thus, Applicant respectfully submits that the cited documents fail to put the public in possession of the claimed invention, and thus, fail to anticipate claims 1-6 (as amended).

The Examiner also rejected claims 54-61 under 35 U.S.C. 102(b) as being anticipated by Sigma Chemical Catalog 1993. Applicant respectfully traverses the rejection.

The rejection is based on the Examiner's interpretation of the claims 54 and 58 as relating to a peptide with as few as two amino acids, an interpretation that was traversed in the remarks regarding the rejection under 35 U.S.C. §112, second paragraph. Moreover, claims 54 and 58 having been amended, Applicant respectfully submits that the rejection has been obviated.

Reconsideration and withdrawal of the rejections under 35 U.S.C. §102 are respectfully requested.

New Claims

Applicant respectfully submits that new claims 62-69 are patentable for at least the reasons discussed herein above for the patentability of, for example, claims 54-61. Entry and consideration of new claims 62-69 are respectfully requested.

Amendment and Response

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Serial No.: 09/991,211

Confirmation No.: 4477

Filed: November 21, 2001

For: CRYSTALLIZATION AND STRUCTURE DETERMINATION OF STAPHYLOCOCCUS AUREUS UDP-N-ACETYLENOLPYRUVYLGLUCOSAMINE REDUCTASE (*S. aureus* MurB)

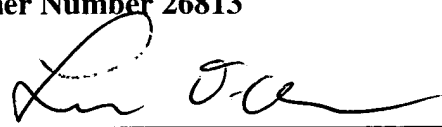
Summary

It is respectfully submitted that all the pending claims are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicant's Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted for
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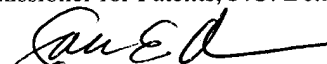
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CERTIFICATE UNDER 37 CFR §1.10:

"Express Mail" mailing label number: EV 405492342 US Date of Deposit: March 1, 2005

The undersigned hereby certifies that this paper is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR §1.10 on the date indicated above and is addressed to **Mail Stop Amendment**, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

By: 
Name: Sara E. OLSON

Amendments to the Drawings

The attached sheet of drawings includes changes to the first sheet of Figure 12. This sheet replaces the original sheet including the first sheet of Figure 12. The first sheet of Fig. 12 has been amended to correct a typographical error, so as to correctly recite Fig. 12A-1 through Fig. 12A-565.